

CONCISE DEFINITIVE REVIEW

Bram Rochwerf, MD, MSc (Epi), FRCPC, Series Editor

Determination of Cerebral Autoregulation at the Bedside: A Narrative Review

OBJECTIVES: To summarize the current evidence on cerebral autoregulation (CAR) monitoring techniques in critical care settings, highlighting their advantages, limitations, and practical applications at the bedside to inform understanding and clinical decision-making for various acute brain injuries and systemic illnesses.

DATA SOURCES: Articles were retrieved using Ovid MEDLINE, PubMed, and Cochrane library using a comprehensive combination of subject headings and key words including “cerebral autoregulation,” “transcranial Doppler,” “near-infrared spectroscopy,” and “intracranial pressure.” See **Supplemental Appendix A** (<https://links.lww.com/CCM/H763>) for complete list of search terms. Relevant articles as well as those discovered through the review process (e.g., references in selected articles) were incorporated into the article.

STUDY SELECTION: Original research, review articles, commentaries, and guidelines focusing on bedside CAR monitoring methodologies, their validation, and applications in critically ill patients were included. The review encompassed both acute brain injury and systemic critical illness conditions.

DATA EXTRACTION: Data from included publications were evaluated and synthesized into a comprehensive narrative review examining CAR monitoring methods and clinical applications.

DATA SYNTHESIS: Three commonly used bedside approaches for assessing CAR were identified. Transcranial Doppler ultrasound measures vessel flow velocity response to blood pressure changes, either through vasopressor administration or monitoring spontaneous fluctuations. Near-infrared spectroscopy evaluates regional cerebral oxygenation changes in response to hemodynamic alterations through continuous, noninvasive forehead sensors. Intracranial pressure monitoring enables assessment of pressure reactivity index through analyzing the correlation between intracranial and arterial blood pressure. CAR impairment is common across critical illness, from acute brain injury to systemic conditions like sepsis, cardiac surgery, and hepatic failure, where dysregulation can lead to secondary brain injury and worse outcomes. While each technique offers unique insights into CAR status, they vary in invasiveness, continuous monitoring capability, and technical requirements. Evidence suggests these methods can help to detect impaired CAR, identify optimal perfusion targets, and may guide individualized management strategies.

CONCLUSIONS: Bedside CAR monitoring represents a promising approach for personalizing hemodynamic management in critically ill patients. While current evidence supports its role in prognostication and management decisions, further research is needed to standardize assessment methods and validate CAR-guided therapy across different critical care conditions. Multimodal monitoring approaches may provide complementary information to optimize patient care.

KEYWORDS: bedside; cerebral autoregulation; intracranial pressure; near-infrared spectroscopy; neuromonitoring; transcranial Doppler ultrasound

Jeffrey R. Vitt, MD¹Spyridoula Tsetsou, MD²Laura Galarza, MD, PhD^{3,4}Aarti Sarwal, MD, FAAN, FCCM,
FNCS, RPN⁵Swarna Rajagopalan^{ID}, MD, MS⁶

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KEY POINTS

Question: What methods exist for bedside determination of cerebral autoregulation status in critically ill patients?

Findings: Numerous bedside techniques have been used to assess cerebral autoregulation at the bedside to prevent and treat primary and secondary brain injury in neurologic and systemic conditions.

Meanings: Cerebral autoregulation can help to triage treatment strategies in critically ill patients with acute brain injury.

Cerebral autoregulation (CAR) is critical in maintaining cerebral perfusion following acute brain injury (ABI) to mitigate the harmful effects of cerebral edema, excitotoxicity, and metabolic mismatch (1, 2). The traditional approach of standardized hemodynamic targets for all forms of acute primary or secondary brain injury (SBI), based on blood pressure (BP) targets presumed to be most favorable on the population level, does not take into account heterogeneous perfusion based on CAR capacity. In the most recent Brain Trauma Foundation guidelines for severe traumatic brain injury (TBI), recommendations were made to maintain a cerebral perfusion pressure (CPP) between 60 and 70 mm Hg, although acknowledgments were made that different targets may be pursued based on CAR capacity that fall outside of traditional targets (3). Mounting evidence highlights the potential benefit of targeting cerebral perfusion thresholds that are specifically tailored to an individual's optimal physiologic characteristics and underlying injury mechanisms (4–6). CAR capacity is increasingly being recognized as a key prognostic factor in ABI as well as SBI in the setting of systemic critical illness, as it influences whether physiologic perturbations can be tolerated or result in permanent injury (7–10). Furthermore, standardized approaches to CAR determination provide an exciting opportunity to guide hemodynamic management using individualized thresholds and assessing response to different targeted interventions (11–14). Several excellent reviews have been published over the past several years covering the emerging clinical role of CAR determination, including evidence supporting different

monitoring modalities, methodologic considerations, and application in diverse clinical situations (15–19). The purpose of this narrative review is to build on this literature by summarizing the current evidence and principles for clinical CAR determination with the goal of providing a practical framework for intensivists to perform CAR assessment at the bedside, and apply it to guide real-time clinical decisions and management.

CEREBRAL AUTOREGULATION PATHOPHYSIOLOGY IN CRITICAL CARE

CAR is a protective mechanism that enables cerebral arterioles to adjust their diameter in response to changes in transmural pressure, maintaining a constant cerebral blood flow (CBF) across varying levels of mean arterial pressure (MAP) or CPP. First described by Lassen (20) in 1959, CAR was initially thought to maintain CBF over a broad BP range (50–150 mm Hg) with the classic curve demonstrating no change in CPP over the CAR plateau across a 100 mm Hg range (**Fig. 1**). When MAP/CPP falls below the lower limit of autoregulation, CBF drops, risking ischemia. When the upper limit is exceeded, hyperperfusion may occur with a risk of cerebral edema and hemorrhage (19, 21). Recent studies suggest the possibility of this plateau extending over a much narrower BP range, of BP closer to 20 mm Hg, with a slightly positive slope, and a directional sensitivity that buffers increases in MAP more effectively than reductions (22, 23). The brain's ability to maintain CPP through such systemic pressure changes also depends on the rate of MAP/CPP variations, with rapid shifts exhausting CAR faster than gradual alterations (21, 24). Modern CAR monitoring relies on spontaneous physiologic BP oscillations in the slow frequency range (Hering-Mayer-Traube waves), which serve as the stimulus for cerebral resistance vessels to produce autoregulatory responses that maintain constant CBF.

ABI from primary neurologic or systemic insult can narrow or eliminate the CAR range and plateau, increasing the risk of cerebral malperfusion from ischemia and/or hyperemia (25–27). This loss of buffering capacity increases the susceptibility to SBI, particularly with fluctuations in MAP (**Fig. 2**). Studies across a range of brain injuries and systemic conditions confirm that the optimal MAP/CPP range for maintaining CAR can vary significantly among individuals, may shift during acute illness within the same patient, and demonstrate a heterogeneous

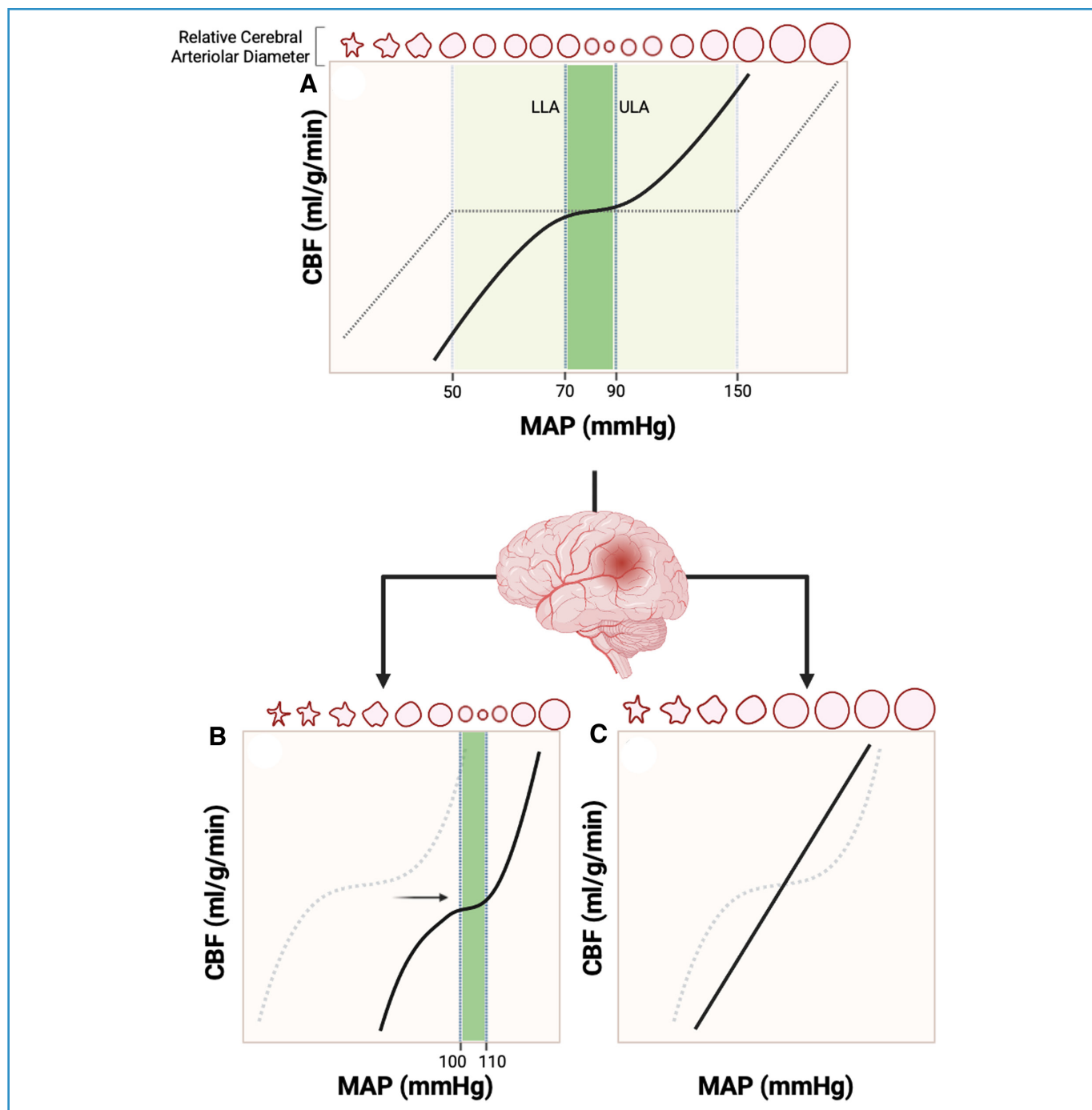


Figure 1. Conceptual models of cerebral autoregulation. Schematic representations of cerebral autoregulation (CAR) illustrating how cerebral blood flow (CBF) is influenced by mean arterial pressure (MAP) under different physiological and pathological states. These models reflect evolving insights into the dynamic and individualized nature of CAR, including deviations from the traditional wide autoregulatory plateau, patient-specific shifts in autoregulatory thresholds, and complete loss of autoregulation in critical illness. The vessel icons in the **top row** of each graph represent cerebrovascular responses—vasodilation and vasoconstriction of arterioles—mediated by intact autoregulatory mechanisms. Together, these panels underscore the clinical relevance of assessing CAR in real time to guide blood pressure targets and optimize cerebral perfusion in vulnerable patients. **A**, Traditional CAR curve showing CBF maintenance across a wide MAP range (50–150 mmHg). The *green shaded region* represents the evolving understanding that autoregulation occurs within a narrower range than classically described, with lower limit of autoregulation (LLA) and upper limit of autoregulation (ULA). **B**, Updated model demonstrating patient-specific autoregulation with a significantly narrower functional range (*green zone*, approximately 100–110 mmHg). This illustrates how autoregulation varies between individuals and can change within the same patient at different stages of illness. **C**, Linear relationship between CBF and MAP representing complete loss of autoregulation, where cerebral perfusion becomes directly dependent on systemic blood pressure (BP) without protective regulation. Created in BioRender (<https://BioRender.com/n6bbvko>).

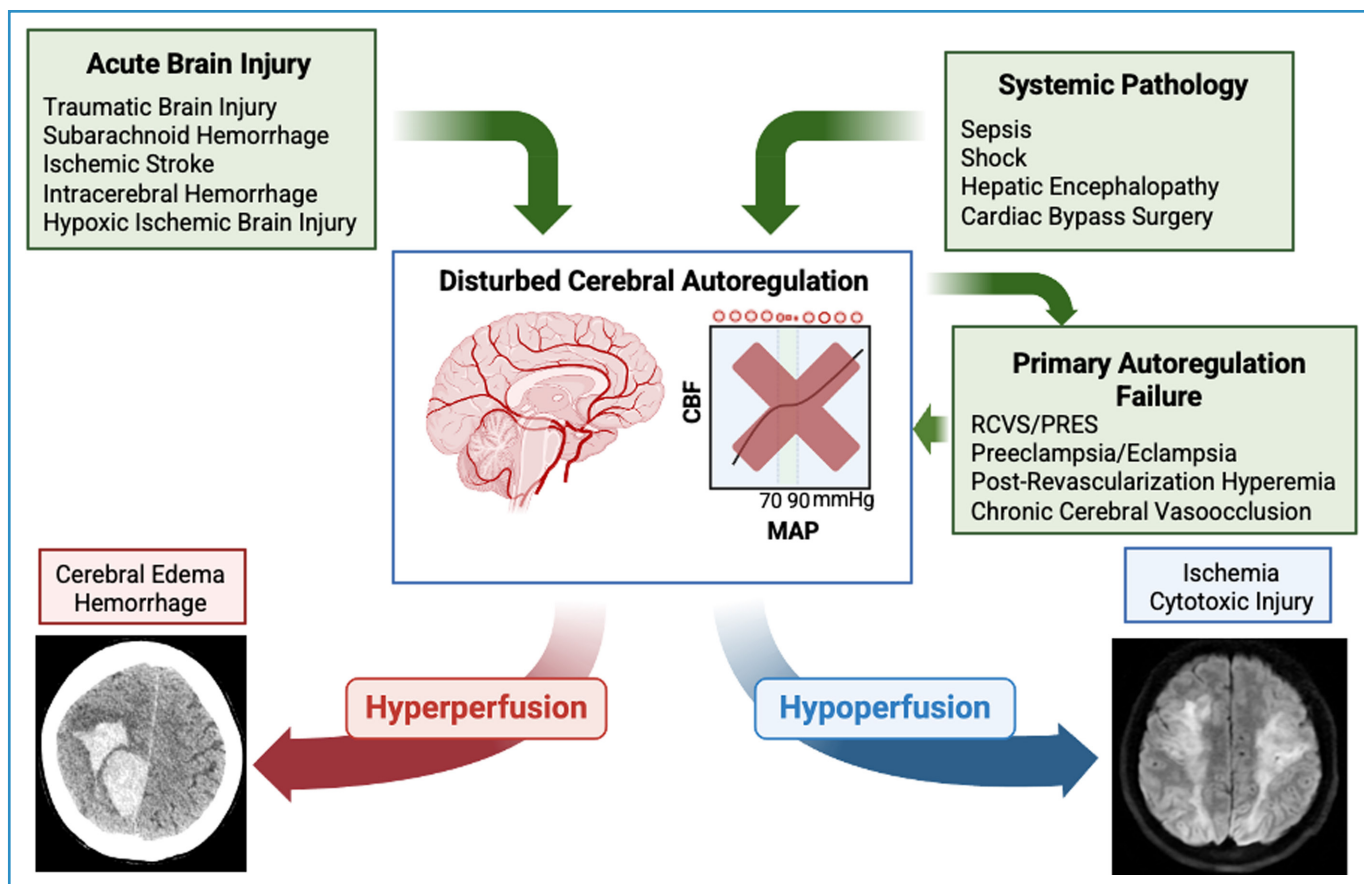


Figure 2. Pathophysiology of disturbed cerebral autoregulation. This diagram illustrates the complex relationships in cerebral blood flow (CBF) dysregulation. The *central blue box* depicts disturbed cerebral autoregulation with a compromised CBF– mean arterial pressure (MAP) relationship (shown by the *red X* over the autoregulation curve between 70 and 90 mm Hg). Two major categories of conditions can cause autoregulatory dysfunction: 1) Acute brain injury (*left green box*): including traumatic brain injury, subarachnoid hemorrhage, ischemic stroke, intracerebral hemorrhage, and hypoxic-ischemic brain injury. 2) Systemic pathology (*upper right green box*): including sepsis, shock, hepatic encephalopathy, and cardiac bypass surgery. Disturbed cerebral autoregulation can result in contribute to the development of diseases characterized by primary autoregulation failure (*lower right green box*), manifesting as conditions like reversible cerebral vasoconstriction syndrome (RCVS), posterior reversible encephalopathy syndrome (PRES), preeclampsia/eclampsia, post-revascularization hyperemia, and chronic cerebral vaso-occlusion. Both disturbed autoregulation and primary autoregulation failure can lead to two distinct pathologic states (*lower portion*): hyperperfusion (*left red pathway*) resulting in cerebral edema and hemorrhage (as illustrated by a CT scan in a patient with reperfusion injury following arteriovenous malformation resection), and hypoperfusion (*right blue pathway*) causing ischemia and cytotoxic injury (demonstrated by MRI, in a patient with watershed infarctions due to Moyamoya disease). These pathways represent the harmful consequences of autoregulatory failure, potentially creating a vicious cycle of progressive brain injury. Created in BioRender (<https://BioRender.com/n6bbvko>).

pattern that differs between hemispheres (**Fig. 3A**; and **Supplemental Fig. 1C**, <http://links.lww.com/CCM/H763>) (25, 28–30). This underscores the importance of evaluating CAR to determine the optimal systemic hemodynamic targets tailored to individual patients, which may differ from commonly used standardized targets.

MEASUREMENT OF CEREBRAL AUTOREGULATION AT THE BEDSIDE

The determination of CAR relies on evaluating the relationship between changes in CBF and MAP. Evaluation

of CAR is broadly classified into intermittent methods, where a MAP change is induced while measuring CBF (directly or indirectly) in one setting, and continuous methods, which monitor spontaneous hemodynamic fluctuations with corresponding CBF changes over longer intervals (31). CAR assessment relies on measurements of CPP and MAP, both of which can be obtained through invasive and noninvasive methods, each with tradeoffs in efficacy, patient safety, spatial, and temporal resolution (32). In the following section, we describe commonly used bedside monitoring modalities for CAR assessment. A summary of

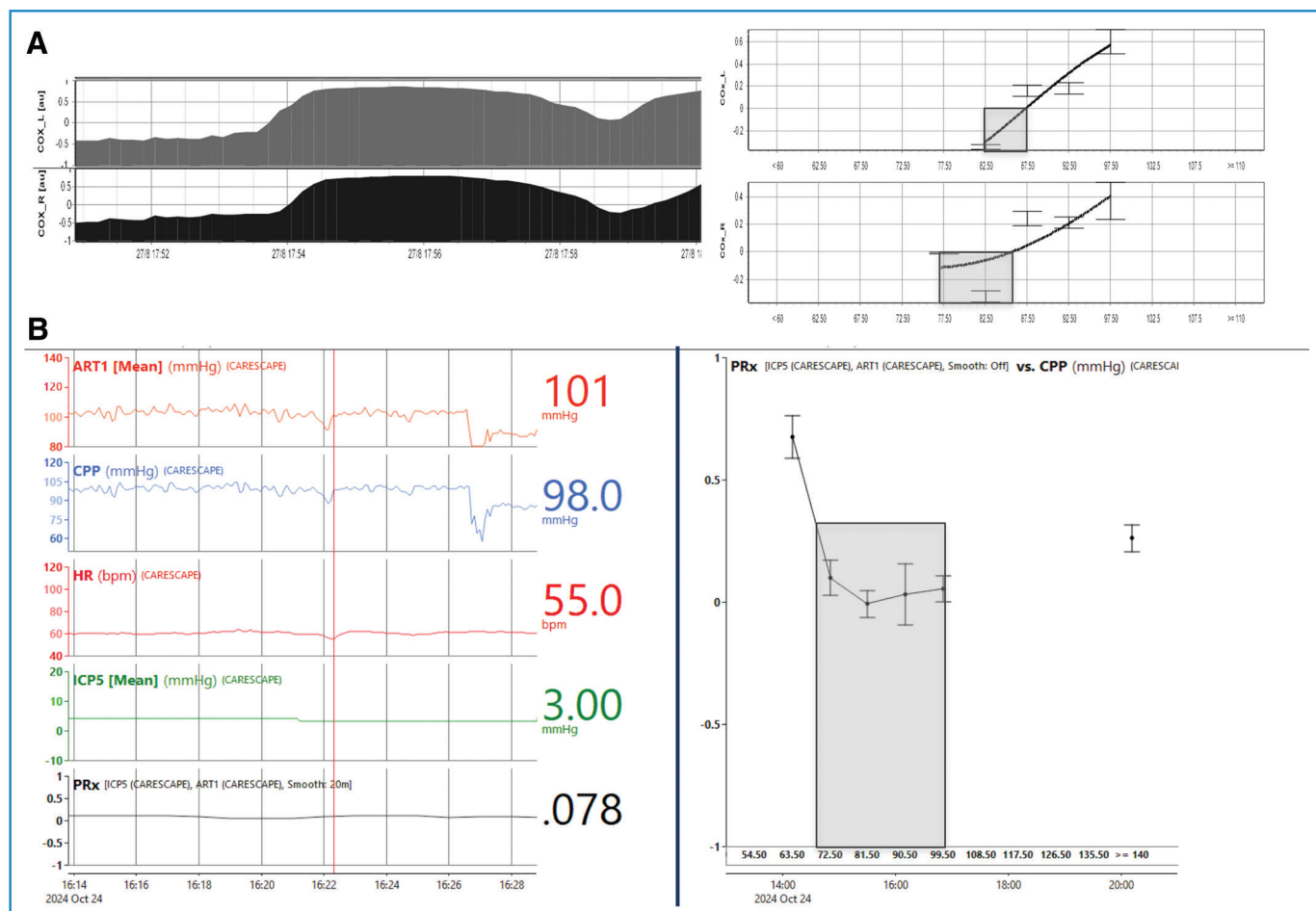


Figure 3. Determination of individual perfusion goals based on autoregulatory status and how individualized cerebral perfusion pressure (CPP) targets can differ from the traditional range of 70–80 mm Hg. **A**, Using near-infrared spectroscopy. The cerebral oximetry index (COx) is plotted over time on the **left**. Initially stable within the autoregulatory range, the COx increases as mean arterial pressure (MAP) exceeds the patient's upper limit of autoregulation, indicating a loss of autoregulation beyond this point. On the **right**, COx is plotted against MAP, showing the overall optimal MAP range of 77–87 mm Hg, where COx is optimal (< 0), but of note, there is variation of cerebral autoregulation (CAR) between hemispheres. **B**, Using intracranial pressure (ICP) monitoring. Despite MAP fluctuations, ICP remains stable, indicating intact CAR with a low pressure reactivity index (PRx) value on the **left**. The **right** depicts the patient's optimal CPP range to be 70–100 mm Hg to maintain a favorable PRx (< 0.3). The lower limit of autoregulation (LLA) is 70 mm Hg, while the upper limit is 100 mm Hg, beyond which CAR is impaired. When CPP falls below the LLA, or rises above the upper limit of autoregulation, the brain may be at risk for ischemia or hyperemia, respectively. ART1 = mean arterial pressure, bpm = beats/min, CARESCAPE = patient monitoring software used in data collection, HR = heart rate. Figure courtesy of Lucia Angelica Rivera Lara, Stanford University, CA.

commonly used CAR indices, associated monitoring modalities, calculation methods, thresholds, and key features is provided in **Table 1**.

Intracranial Pressure Monitoring

Intracranial pressure (ICP) monitoring is an invasive technique, typically involving an external ventricular drain or parenchymal probe, commonly used in severe ABI patients. ICP has long been used as a surrogate for CBF, assuming decreased intracranial compliance,

where changes in MAP may result in CBF alterations and lead to corollary fluctuations in ICP (9, 48).

A practical intermittent method for bedside CAR assessment involves a MAP challenge by using a vasopressor to raise MAP by 10–20% from baseline and observing ICP changes after approximately 5 minutes to allow for steady state: an ICP increase suggests impaired CAR, while stable or reduced ICP despite increase in MAP indicates intact CAR (**Supplemental Fig. 1, A and B**, <https://links.lww.com/CCM/H763>) (33). For patients where cerebral hyperemia may be

TABLE 1.**Cerebral Autoregulation Monitoring: Tabulated Assessment Indices, Measurements, Characteristics, and Treatment Thresholds With Pros and Cons Related to the Modality**

Index	Device	Duration	Calculation	Threshold	Key Features
MAP challenge (22, 33)	ICP $\pm$ PbtO ₂ monitors	≤ 20 min	ICP $\uparrow$ = impaired	Not applicable	Direct; invasive
PRx (34–36)	ICM+, Moberg	4 min	r = ICP/MAP; 10 s averages $\times 30$	> 0.2 : $\uparrow$ Mortality and poor outcome	Validated; invasive; infrastructure needed
Oxygen reactivity index (37, 38)	ICM+, Moberg	60 min	r = PbtO ₂ /CPP; 30 s averages	> 0.3 – 0.4 : Poor outcome	Oxygen-based; invasive
Flow-related autoregulation index (39)	Thermal-diffusion–rCBF	Min	r = rCBF/CPP	Correlation w/Mx	Direct CBF; regional
Static rate of regulation (33, 40)	TCD	Min	$\Delta CVR_e/\Delta ABP$	> 0.4 – 0.6 : intact	Noninvasive; operator dependent
Sx (41)	TCD	≥ 50 min	r = flow velocity systolic/CPP	> -0.2 : $\uparrow$ Mortality, > -0.15 poor outcome	Noninvasive; operator dependent; infrastructure needed Sx, Sx_a closest TCD-based surrogate to PRx
Sx_a (41)	TCD	≥ 50 min	r = peak systolic velocity/MAP	> 0.05 : $\uparrow$ Mortality, > -0.1 poor outcome	
Mx (42)	TCD	≥ 30 min	r = MFV/CPP	> 0.3 : $\uparrow$ Mortality and poor outcome	
Mx_a (42)	TCD	≥ 30 min	r = MFV/MAP	> 0.3 : Poor outcome	
Dynamic rate of regulation (33)	TCD, tight leg-cuff release	5 min	Flow restore rate	Normal: 20%/s	Complex signal processing; noninvasive; metabolite affect cerebrovascular resistance; operator dependent
Autoregulation index (33)	TCD, tight leg-cuff release	5 min	CBF response model fit	0–9 scale; 0-absent and 9-intact	
Transient hyperemic response ratio (43)	TCD, carotid compression	30 min	Hyperemic ratio	< 1.1 : impaired	Embolism risk; noninvasive
Cerebral oximetry index (44, 45)	Near-infrared spectroscopy +		r = regional oxygen saturation/MAP	(+) impaired	Limited data; noninvasive; inconsistent across devices
Tissue oxygenation reactivity index (46)	ICM+		Tissue oxygenation index/CPP	(+) impaired	
Hemoglobin reactivity index (47)	1 hr		Total hemoglobin/MAP	(+) impaired	

CBF = cerebral blood flow, CPP = cerebral perfusion pressure, ICM+ = Integrated Cerebral Monitoring Platform (Cambridge) (1), ICP = intracranial pressure, MAP = mean arterial pressure, MFV = mean flow velocity, Moberg = CNS Monitor for Multimodal Data Acquisition (2), Mx/Mx_a = correlation indices using mean flow velocity with cerebral perfusion pressure/mean arterial pressure, PbtO₂ = brain tissue oxygen tension, PRx = pressure reactivity index, r = correlation analysis, rCBF = regional cerebral blood flow, Sx = systolic flow index using flow velocity systolic/cerebral perfusion pressure, Sx_a = systolic flow index using flow velocity systolic/mean arterial pressure, TCD = transcranial Doppler, ΔABP = change in arterial blood pressure, ΔCVR_e = change in effective cerebrovascular resistance.

Detailed static rate of regulation (sROR) calculation: $sROR = (\Delta CVR_e/\Delta ABP)$ with $\Delta CVR_e = (CVR_{e2} - CVR_{e1})/CVR_{e1}$ and $\Delta ABP = (ABP2 - ABP1)/ABP1$, with 0% for full compensation and 100% for no compensation.

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contributing to increased ICP, reducing MAP can clarify if elevated ICP results from excess perfusion, although CPP should be maintained above 60 mm Hg to avoid ischemia (5, 49). With either maneuver, it is important that external stimulation is minimized and end-tidal CO_2 is kept constant throughout the intervention to ensure valid results (22).

A continuous method of integrating systemic BP and ICP using time-correlation analysis can yield CAR measured as the pressure reactivity index (PRx). PRx is calculated as the moving correlation coefficient between ICP and spontaneous slow frequency oscillations in MAP, mediated by baroreflex activity and sympathetic tone, to produce a continuous CAR assessment. Higher positive PRx values indicate impaired CAR, while close to zero or negative values suggest intact autoregulatory function (**Supplemental Fig. 3**, <https://links.lww.com/CCM/H763>) (32).

The invasive nature of ICP monitoring limits its use in patients, with complications (e.g., misplacement, infection, hemorrhage) occurring in 14–38% of cases, particularly in those with cerebral edema and midline shift (50–52). Importantly, PRx assesses cerebrovascular reactivity through ICP changes that reflect cerebral blood volume alterations, which differs fundamentally from transcranial Doppler (TCD) ultrasound and near-infrared spectroscopy (NIRS) that measure direct surrogate markers of CBF. PRx depends on compromised intracranial compliance for small alterations in CBF to impact ICP and may be inconclusive in patients without sufficient mass effect (31, 51). Additionally, since ICP reflects the global summation of supratentorial pressures, PRx likewise lacks spatial resolution to detect heterogeneous CAR patterns that may vary across different parts of the brain (53, 54).

Transcranial Doppler Ultrasound

TCD is a portable, noninvasive modality that directly measures CBF velocity (CBFV) as a surrogate for CBF, assuming vessel radius remains constant during the study (55, 56). Rate of regulation (ROR) provides CAR assessment during a MAP challenge by using a vasopressor to increase MAP 10–20% above baseline while monitoring TCD-derived mean CBFV of the middle cerebral artery (MCA), similar to the MAP challenge with ICP monitoring described above, and illustrated in **Figure 4** (33). ROR ranges from 0 (absent CAR) to 1 (excellent CAR), with a reported 0.4–0.6 cutoff across multiple studies

indicating exhausted CAR (40, 56–58). As previously mentioned, maintaining a stable PaCO_2 throughout the recording is crucial for reliable results as ROR can be erroneous with hypercapnia in both healthy and ABI subjects (59). In the setting of disturbed CAR, bedside TCD can also be helpful in characterizing whether the pattern of perfusion abnormality is related to ischemia and oligemia or hyperemia (**Supplemental Fig. 2**, <https://links.lww.com/CCM/H763>). Other provocative maneuvers, like the carotid compression test, can be performed at bedside and are designed to induce abrupt changes in MAP to characterize CAR. This can be performed by compressing the common carotid artery, resulting in an approximate 50% drop in ipsilateral MCA CBFV for 10 seconds, followed by release of pressure. A transient hyperemic response in the MCA denotes intact CAR (due to vessel vasodilation), whereas an immediate return to baseline suggests impaired CAR and can be quantified via the transient hyperemia response ratio (60). It is important to note that results may be confounded by preexisting carotid disease or collateralization and rapid changes in MAP may not be advisable in certain vulnerable ABI patients where there is increased risk of ischemia and infarction.

Continuous assessment of CAR can also be done by analyzing CBFV responses to spontaneous hemodynamic oscillations through time-correlation analysis similar to PRx (31, 61). The moving correlation coefficient of MAP/ CPP and continuous MCA CBFV yields mean flow index (Mx) and systolic flow index (Sx), depending on whether mean-flow velocity or peak systolic velocity is the chosen dependent variable respectively, where positive values suggest impaired CAR and near-zero or negative values denote intact function (62, 63). Mx and Sx correlate well with CAR indices derived from other modalities and have been validated across a wide range of conditions (41,64–68).

TCD is limited by inadequate sonographic windows in approximately 10–15% of subjects and difficulty with probe placement, which hinders continuous monitoring (69, 70). Recent advances in robotic headset technology now allow semi-intermittent TCD monitoring for hours, improving temporal resolution and making TCD more viable for extended ICU monitoring (71, 72).

Near-Infrared Spectroscopy

NIRS is a noninvasive modality that measures regional cerebral oxygenation and provides an indirect

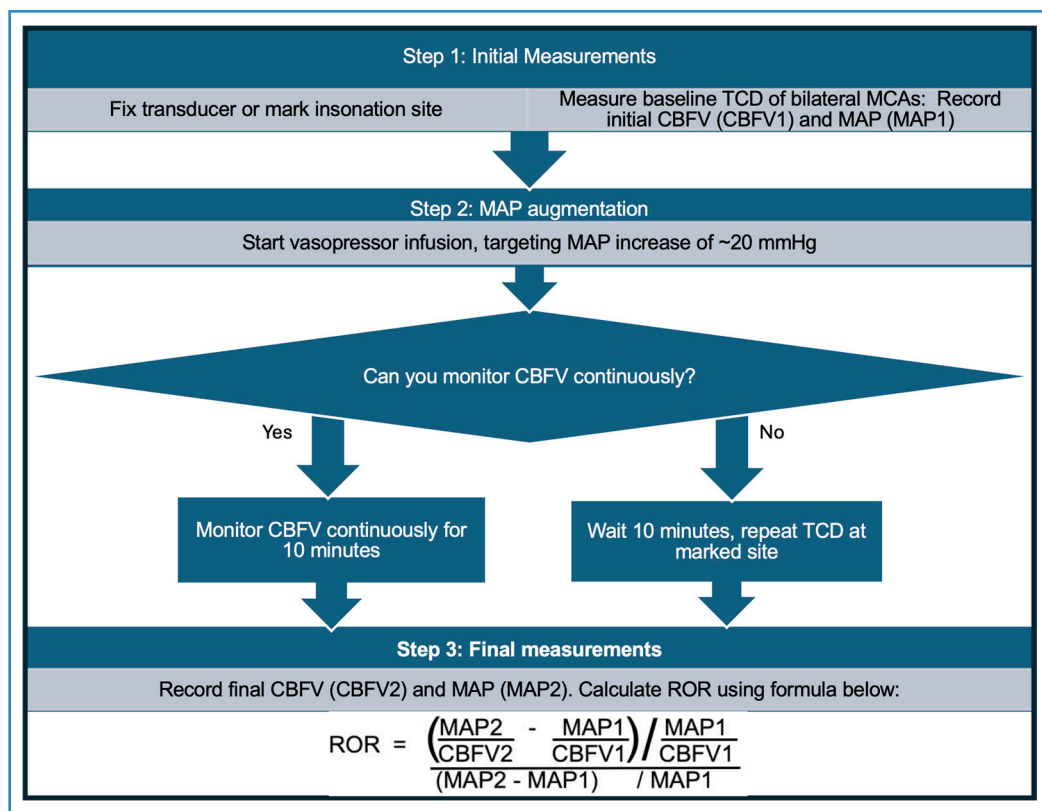


Figure 4. A step-by step flowchart of bedside cerebral autoregulation assessment using transcranial Doppler ultrasonography. CBFV = cerebral blood flow velocity, MAP = mean arterial pressure, MCA = middle cerebral artery, ROR = rate of regulation, TCD = transcranial Doppler.

assessment of CBF by emitting near-infrared (NIR) light (650–950 nm) through the cortex, skull, and skin (73). Forehead optodes detect NIR light attenuation, estimate oxygenated hemoglobin (HbO), deoxygenated hemoglobin, total hemoglobin index, tissue oxygenation index (TOI), and regional cerebral oxygen saturation (rSO₂) (74). Unlike TCD, NIRS requires no specialized training, making a practical and accessible choice for continuous ICU monitoring (75). In pediatrics, NIRS has been used for continuous CAR assessment by tracking HbO changes in response to a MAP challenge induced by phenylephrine (76, 77). NIRS-derived CAR indices, such as cerebral oximetry index, tissue oxygen reactivity index, and total hemoglobin reactivity index (Fig. 3A), show good correlation with established methods like PRx and Mx and may provide complementary cortical arteriole-level CAR monitoring (46, 78–83). The ability to place optodes over different regions of interest is another advantage of NIRS and enhances the spatial resolution of CAR in distinct cortical locations (84). However, accurate NIRS signals require proximity to the cortex and may be unreliable in settings with pneumocephalus, scalp edema, contusions, and hemorrhage

(85). Skin pigmentation also affects signal reliability and is a major drawback of the technology (86). Additionally, the lack of standardization across different NIRS devices leads to discrepancies in measurements (e.g., rSO₂ and TOI) and derived indices, despite being based upon the same underlying physiologic principles. These metrics have not been rigorously cross-validated between manufacturers, thereby limiting the generalizability and comparability of study findings across different devices and clinical settings (75, 87).

CEREBRAL AUTOREGULATION AS A PHYSIOLOGIC TARGET—LESSONS FROM ACUTE BRAIN INJURY

Prognostication

Impaired CAR serves as an important prognostic marker for mortality and neurologic outcome across a spectrum of ABI subtypes. In severe TBI, PRx thresholds, measured around 1 week post injury, have been shown to be associated with functional outcomes (PRx +0.05–0.325) and mortality (PRx > +0.25–0.35) (42, 88, 89). TCD-derived indices in TBI have similarly demonstrated increased mortality risk at Mx above +0.3 while the threshold for Sx has been reported at –0.2, highlighting that distinct thresholds exist across different indices (54, 90). Furthermore, in subarachnoid hemorrhage (SAH), higher PRx values (+0.5–0.75) correlate with poorer outcomes, similar to those observed in TBI. However, extreme negative PRx values, possibly from vascular hyperactivity with reduced CBF, are also associated with unfavorable outcomes in SAH and support the existence of disease-specific optimal thresholds (90, 91).

Guiding Clinical Management

CAR assessment is a valuable tool for ICU decision-making. Bedside determination of impaired CAR can predict ICP increases during MAP augmentation, suggesting a pressure-passive state, with corresponding deterioration of cerebral oxygenation (40, 59). In TBI with elevated ICP, PRx outperforms fixed ICP thresholds (20–25 mm Hg) in predicting harm, supporting individualized therapy based on CAR (92). In SAH, impaired CAR on TCD and NIRS often aligns with severe vasospasm, helping identify patients at risk for developing delayed cerebral ischemia who may benefit from CBF augmentation (68, 84, 93). Similarly, elevated Mx in intracerebral hemorrhage and following endovascular revascularization in large-vessel ischemic stroke may predict hematoma expansion and malignant cerebral edema, respectively, thus identifying patients at risk for decompensation and guiding hyperosmolar therapy (25, 66).

Optimal Perfusion Targets

Perhaps the most exciting potential of CAR monitoring is the opportunity to tailor hemodynamic targets to individual physiology rather than standardized thresholds. By continuously trending CAR indices against perfusion pressures, a U-shaped curve can be constructed where the lowest index value denotes the most intact CAR and thus the “optimal” MAP or CPP (MAP_{OPT} or CPP_{OPT}) (Fig. 3) (11, 94). Data from healthy subjects reveals considerable variability in MAP_{OPT} values, likely reflecting baseline in systemic and cerebrovascular physiology (95). These findings support the concept that optimal cerebral perfusion may require individualized BP targets. Identifying and maintaining optimal perfusion targets appears to be particularly important in the context of intracranial pathology. In TBI, studies have shown that aligning CPP with CPP_{OPT} improves cerebral metabolism and outcomes (53, 96–98). Similarly, in SAH with vasospasm, PRx-guided hemodynamic augmentation has led to improved cerebral oxygenation and CBF over standard MAP thresholds (28, 99). Noninvasive indices derived from TCD and NIRS also offer methods for the determination of MAP_{OPT} , with overall good agreement with PRx-derived targets, and evidence in TBI populations that deviations of more than 10 mm Hg on average from determined goal thresholds correlate

with worse outcomes (63, 72, 100). While promising, CAR-guided therapy in ABI lacks prospective evidence. Early studies have demonstrated the feasibility and safety of aligning blood pressure targets with individual autoregulatory thresholds in TBI, but have been underpowered to assess clinical benefit, highlighting the need for further research (101).

POTENTIAL OPPORTUNITIES FOR AUTOREGULATION MONITORING IN SYSTEMIC CRITICAL ILLNESS

Septic Encephalopathy

Septic encephalopathy is one of the most common neurologic manifestations in sepsis, associated with a risk of long-term cognitive impairment (102). CAR is often impaired in septic encephalopathy, with dysfunction proportional to illness severity, and has been correlated with the development of delirium presumably through microvascular dysfunction and malperfusion (103, 104). Determination of MAP_{OPT} is feasible in this condition, and deviations from optimal values have been associated with a lower Glasgow Coma Scale score (105).

Hypoxic-Ischemic Brain Injury

Following hypoxic-ischemic brain injury, CAR dysfunction is common, particularly in patients with severe brain injuries or chronic hypertension, and can be further exacerbated during hypothermia or with hypercarbia (29, 106, 107). While higher MAP is generally associated with improved outcomes, controlled studies targeting higher MAP targets have not found a benefit (108–110). In keeping with other forms of ABI, optimal MAP following cardiac arrest appears to be highly variable, making a standardized approach challenging and underscores the necessity for bedside assessment methods to guide hemodynamic decisions (29).

Cardiopulmonary Bypass and Venoarterial Extracorporeal Membrane Oxygenation

In patients undergoing cardiopulmonary bypass during cardiac surgery, CAR appears to be a strong predictor of postoperative complications. This was recently evaluated in a systematic review where impaired postoperative CAR increased the risk of adverse events including stroke, delirium and mortality (111). The impact of CAR in patients undergoing extracorporeal membrane

oxygenation is still incompletely understood. In a recent study of 13 patients, it was found that patients who remained comatose had higher hemispheric asymmetry in TCD-derived CBFV, although the clinical relevance of this finding remains unclear (112).

Hepatic and Uremic Encephalopathy

In patients with hepatic encephalopathy, dysregulated cerebral vascular tone with resulting hyperemia has been demonstrated as an important basis for the development of potentially fatal cerebral edema and elevated ICP (113). A decrease in cerebrovascular reserve and CAR capacity has been identified in patients with decompensated cirrhosis, although this appears to be reversible following clinical stabilization as well as after transplantation (114, 115). Other investigations have demonstrated the feasibility of continuous CAR monitoring during orthotopic liver transplantation, which may prove useful for determining hemodynamic targets and implementing neuroprotective strategies in the perioperative and operative settings to maximize the potential for recovery (67, 116). Renal and brain dysfunction are tightly correlated with evidence of cerebral microcirculation dysfunction, inflammation, and neurotransmitter dysregulation. Initiation of hemodialysis is a risk factor for disturbed CAR with risk of cerebral malperfusion, edema formation, and herniation and may be predicted with the use of noninvasive modalities such as TCD (117).

Peripartum Neurologic Disorders

In pregnant patients, CAR is critical for protecting the maternal brain against acute and drastic changes in total circulating blood volume and MAP. In the case of preeclampsia and eclampsia, CAR dysfunction has been demonstrated to correlate with overall severity and likely contributes to neurologic manifestations of cerebral edema and seizures (118).

FUTURE DIRECTIONS

The evolving landscape of CAR monitoring offers significant potential for improving patient outcomes in critical care. However, variability between CAR assessment methods currently limits their interchangeability. Simple steady state approaches, such as MAP challenge, do not take into account dynamic fluctuations

critical to CBF homeostasis, whereas continual monitoring approaches, including PRx and Mx, require complex computational analysis that limits practicality in most medical settings. Future research should aim to develop rapid, accessible methods for continuous CAR assessment, while deepening the understanding of CAR's role across different disease states, as optimal thresholds vary person to person. Longitudinal studies examining CAR dynamics over time, particularly in response to interventions like fluid resuscitation or vasopressor therapy, could yield insights into the temporal characteristics of autoregulation and its implications for hemodynamic management. With emerging therapies like CAR T-cell therapy and lecanemab, which are linked to cerebral edema, investigating their impact on CAR is crucial. Furthermore, future investigations should assess the utility of CAR monitoring in the perioperative setting, particularly during cardiac surgery and liver transplantation to help improve neurologic outcomes.

Finally, establishing standardized protocols for CAR assessment using diverse methodologies—including TCD, NIRS, and ICP monitoring—will enhance the comparability of research findings and facilitate the development of universal guidelines. As the field advances, embracing a multimodal approach to CAR monitoring that complements each other could lead to significant improvements in the management of patients with acute brain injuries and systemic critical illnesses, ultimately translating to better clinical outcomes.

CONCLUSIONS

The expanding role of bedside CAR assessment techniques offers a unique opportunity to enhance individualized care for patients with ABI and systemic critical illness. By refining hemodynamic targets based on real-time autoregulatory capacity, CAR monitoring can move beyond standardized thresholds, potentially improving outcomes across a diversity of conditions. Achieving this potential requires further innovation in continuous, noninvasive CAR assessment methods and integration into clinical practice, paving the way for a new era in critical care management.

1 Department of Neurological Surgery and Neurology, UC Davis Medical Center, Sacramento, CA.

2 Department of Neurology and Neurosurgery, Baylor College of Medicine, Houston, TX.

- 3 Department of Intensive Care, Hospital General Universitario de Castellón, Castellón de la Plana, Spain.
- 4 Department of Medicine, University Jaume I (UJI), Castellón de la Plana, Spain.
- 5 Department of Neurology, Virginia Commonwealth University School of Medicine, Richmond, VA.
- 6 Department of Neurology, Cooper Medical School of Rowan University, Camden, NJ.

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For information regarding this article, E-mail: rajagopalan-swarna@CooperHealth.edu

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